REMARKS

In view of the preceding amendments and the comments which follow, and pursuant to 37 CFR §1.111, amendment and reconsideration of the Official Action of June 24, 2005 is respectfully requested by Applicants.

The specification has been amended to insert missing serial numbers in paragraph 114. No new matter has been added.

Claims 6 and 7 have been cancelled. Claims 1, 22, 29, 33, and 36 have been amended. Support for the recitation "one of which is directly linked to the phenyl ring" added to claims 1, 22, and 29 is found throughout the specification and in the drawings where the haptens, immunogens, and labels of the present invention are described. All the structures depict L linked to the ring via a carbon atom. Support for the language added to claims 33 and 38 is found in the originally filed specification in paragraphs 28 and 79. No new matter has been added.

Claims 1-3, 5, 10, 11, 13, 14, 16-33, and 36 remain pending for examination.

Amendments to specification

The examiner has noted that serial numbers are missing from the text on at least pages 34 and 35, and she requires correction. She also suggested that Applicants thoroughly check the specification for the possibility of other missing data.

In accordance with the examiner's request, Applicants have amended their specification accordingly and have checked the specification to assure that no additional data is missing.

Rejection under 35 USC §112, first paragraph

Claims 10, 11, 13, and 14 have been rejected under 35 USC §112, first paragraph, as failing to comply with the enablement requirement. The examiner remarks that Applicants have not established that the cell lines and antibodies designated in these claims are accessible to the public in accordance with the requirements of MPEP 2404-2411.

In response, Applicants submit the attached Declaration of Biological Deposit, and the examiner's reconsideration of the rejection is respectfully requested.

Rejection under 35 USC §112, second paragraph

Claims 33 and 36 have again been rejected under 35 USC §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as their invention.

The examiner argues that claims 33 and 36 are indefinite and incomplete for failing to define how the "complex" formed by the antibody and the analyte is to be detected, and it is unclear what is meant to be encompassed by the term "a label which is detectable upon binding of the antibody to the analyte".

Applicants have amended claims 33 and 36 to recite the step of contacting the sample with the antibody and a "conjugate comprising an analyte analog and a detectable label, whereby the analyte and the analyte analog compete for binding to the antibody" and the step of "measuring the labeled conjugate bound to the antibody or measuring the unbound labeled conjugate as a measure of the analyte in the sample".

The examiner's reconsideration of the rejection under 35 USC §112, second paragraph, is respectfully requested.

Rejection under 35 USC §112, first paragraph

Claims 1-3, 5-7, 16-33, and 36 have been rejected under 35 USC §112, first paragraph, as failing to comply with the written description requirement. The examiner argues that the specification contains no description of the subset of compounds in which L contains a proviso wherein L is bound to the ring carbon via $-CH_2-$ or $-CH_2O-$.

Applicants have now amended independent claims 1, 22, and 29, from which the remaining rejected claims depend, to recite that one of the L carbon atoms is directly linked to the phenyl ring, thereby avoiding the rejection.

The examiner's reconsideration of the rejection under 35 USC §112, first paragraph, is respectfully requested.

Double patenting rejections

Claims 10, 11, 13, 14, 16-28, 33, and 36 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 17, 18, 31, and 42-44 of copending application no. 10/087,469. For reasons cited in the previous action, the examiner argues that, although the conflicting claims are not identical, they are not patentably distinct from each other because the claimed antibodies of both applications have the same specificity, i.e., for MDEA.

Applicants have now cancelled claims 17, 18, 31, and 42-44 in copending application no. 10/087,469, thereby avoiding the rejection.

Claims 10, 11, 13, 14, and 16-28 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 8 and 9 of copending application no. 10/622,254. For reasons cited in the previous action, the examiner argues that, although the conflicting claims are not identical, they are not patentably distinct from each other because the claimed antibodies of both applications have the same specificity, i.e., for MDEA.

Applicants inform the examiner that claims 8 and 9 are now pending in a divisional of copending application no. 10/622,254, namely application no. 11/076,569. Further, Applicants traverse the rejection on the grounds that the claims in question are drawn to different, specific cell lines and antibodies produced from those cell lines. The various cell lines were developed from different immunogen structures and should be patentably distinct. Further, there are differences in antibody characteristics recited in the claims, e.g., they are characterized by "preferentially" binding or having a defined amount of "cross-reactivity" to various drugs of the ecstasy class. Specificity and preferential binding are defined in paragraphs 40 and 42 of the instant application. Applicants still assert, as they have previously, that a terminal disclaimer will be filed in the event any of the provisionally rejected claims are in conflict at the time of patenting; however, Applicants interpret "in conflict" to mean that such claims are not patentably

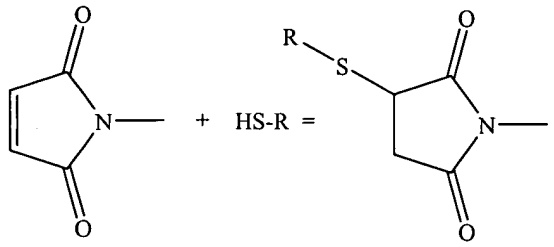
distinct. The examiner's reconsideration of which claims are not patentably distinct in the two applications is respectfully requested.

Rejection under 35 USC §102 (b)

Claims 1-3, 5-7, 22-25, 29-33, and 36 have been rejected under 35 USC §102 (b) as being anticipated by Huber et al (US 5,976,812, hereinafter "Huber. The Examiner argues that Huber describes *para*-derivatized amphetamine haptens wherein the linker contains carbon atoms and optionally heteroatoms and is attached directly to the benzene ring; these activated haptens are useful in preparing the corresponding amphetamine immunogens, antibodies, and tracers and anticipate the corresponding immunogens, tracers, antibodies, and their method of use in an immunoassay of the instant claims wherein L comprises 1-15 carbon atoms and 0-6 heteroatoms. See Huber, structures 13, 14, and 16-18. The examiner also argues that claims 7 and 25 contain the added limitation that R1 is ethyl and R2 is methyl, i.e., the terminal amine group is –N(Et)Me. Huber specifically describes this compound limitation at column 2, lines 32-47, wherein R4 and R5 can be methyl or ethyl, i.e., the terminal amine group is –N(Et)Me. Therefore, the examiner's position is that Huber anticipates the instant claims.

In this regard, the examiner has found Applicant's previous argument, i.e., that the compounds described by Huber are all maleimide derivatives and therefore cannot anticipate the compounds of the instant invention, to be unpersuasive for the reason that the maleimide moiety of Huber corresponds directly to the Q moiety of claim 1 defined as a leaving group.

Applicants respectfully argue that the examiner's reasoning for finding Applicants' previous arguments to be unpersuasive to be in error. Maleimide is not a leaving group. Applicants have defined a leaving group in paragraph 38 of their specification as any chemical moiety of a substrate that can be displaced by a reagent reacted therewith, and they have provided numerous examples. Maleimide is a thiol reactive group. It has a specific structure and will react with nucleophiles, typically a thiol, where the nucleophile adds to the double bond to form a covalent bond to the ring. Maleimide is not displaced, i.e., it does not "leave":



Further in an effort to eliminate the issues that remain in the present application, Applicants have now amended their claims by canceling claims drawn to activated hapten derivatives. Applicants compound claims now are drawn to immunogen and labeled conjugates. In light of the present amendments and the above explanation as to why the examiner's reasoning is in error, Applicants respectfully request the examiner's reconsideration of the rejection and reconsideration of the arguments put forth by Applicants in their previous reply. The structures taught by Huber are amphetamine derivatives. See the structure at column 2, line 40, and Figure 2, structures 15-17. These structures are all maleimide derivatives, however, and therefore cannot anticipate the compounds present invention. Furthermore, the structures taught by Huber do not make the compounds of present invention obvious because Huber contains no teaching that would lead to the derivatives of the present invention, nor does Huber teach the benefit of using N-ethyl amphetamine derivatives to obtain antibodies specific for MDEA as taught by the present invention. It follows, therefore, that the antibodies, kits, and methods of the present invention are likewise neither anticipated nor made obvious by the disclosure of Huber.

Rejection under 35 USC §102/103 (a)

Claims 10, 13, and 16-28 have been rejected under 35 USC §102/103 (a) as being unpatentable over Huber for the reason stated in the previous rejection. The Examiner argues that in absence of evidence to the contrary, the antibodies and cell lines (col. 5, lines 60-14) of the prior art are considered to have the same characteristics recited for the cell lines and antibodies of the instant claims 10, 13, and 16-21.

Applicants respectfully traverse the rejection and argue that that the compounds taught by Huber (specifically, Huber's compounds 9 and 18) produce antibodies to amphetamine and methamphetamine (see Examples 4 and 5 in Huber). There is no evidence to show that such antibodies are also specific for MDEA, nor is there any reason for the skilled artisan to expect

that antibodies produced from Huber's maleimide derivatives would produce the highly specific antibodies achieved by the Applicants using the immunogen of their invention. Further, there is no reason to expect that the prior art immunogens of Huber would produce antibodies that preferentially bind MDEA relative to other members of the ecstasy class of drugs.

Applicants were attempting to solve the problem of providing antibodies with specificity for MDEA when they made their discovery that, by removing a portion of the MDEA molecule, i.e., the methylene dioxy moiety, and then making a substitution off the benzene ring and adding a single carbon off the benzene nitrogen (going from a methyl to an ethyl group), they were able to achieve antibodies with a high specificity for MDEA. There is no reason taught by the prior art that would lead the skilled artisan to expect that, when a portion of the MDEA hapten molecule is removed, production of antibodies highly specific for the original molecule are achievable. This result was surprising and unexpected.

In light of these remarks and the present amendments, the examiner's reconsideration of the rejection is respectfully requested by Applicants.

Rejection under 35 USC §103 (a)

Claims 1-3, 6, 11, 14, 16-25, 26-28, 29, 32, 33, and 36 have been rejected under 35 USC §103 (a) as being obvious over each of Gross (US 3,996,344, hereinafter "Gross"), Soares (US 4,016,146, hereinafter "Soares"), Buechler et al (US 5, 470,997, hereinafter "Buechler"), Huber et al (US 5,976,812, hereinafter "Huber"), Heiman et al (US 5,262,333, hereinafter "Heiman"), Hu et al (US 5,135,863, hereinafter "Hu"), Byrnes et al. (US 4,868,132, hereinafter "Byrnes"), or Schneider et al (US 3,878,187, hereinafter "Schneider"). The Examiner argues that each of the references describes methamphetamine derivatives in which the phenyl ring is substituted at the *para* position with an activated linker moiety. The linker moiety can be reacted with an immunogenic carrier or label to form the corresponding *para*-substituted methamphetamine immunogen or detectably labeled methamphetamine derivative. The examiner's opinion is that the compounds of the references differ from those of the instant claims in that at least one moiety on the nitrogen atom of the compounds of the instant claims is an alkyl group of from "2-6" carbon atoms" while at least one moiety on the nitrogen of the prior art is 1 carbon atom in

length. The *para*-substituted activated haptens, immunogens and tracers of the instant claims wherein the nitrogen is ethyl (through hexyl)-substituted are rendered obvious by the structurally related methyl homologs of the prior art. The examiner's position, therefore, is that, absent evidence to the contrary, the claimed compounds would be expected to have very similar properties to the compounds of the prior art. Given the structural similarities of the haptens of the instant invention and those of the prior art, the antibodies of the prior art would be expected to inherently have the same specificity for MDEA as the antibodies of the instant claims.

Applicants traverse the rejection and respectfully argue that, although the cited references disclose a *para*-substituted phenyl ring, none of the references (with the exception of Huber who is discussed above) disclose or suggest N-ethyl substituted derivatives. Further none of the references suggest the advantages of using N-ethyl amphetamine conjugates to obtain antibodies that specifically and preferentially bind MDEA, nor do the references provide the motivation for a person skilled in the art to try using N-ethyl amphetamine conjugates to obtain antibodies that specifically and preferentially bind MDEA.

The examiner argues that the antibodies of the prior art would be expected to inherently have the same specificity for MDEA as the antibodies of the instant claims. However, as previously argued by Applicants, the examiner's attention is drawn to the antibody characteristics taught by Heiman in Table 2, columns 21 and 22. Although Heiman's antibody will detect MDEA, the antibody is neither specific nor preferential for MDEA, nor would it be suitable for use in an assay to determine MDEA in a sample. Thus, it cannot be logically assumed that any antibody produced in response to an immunogen derived at the *para* position of amphetamine will have the same specificity for MDEA as the antibodies of the present invention. In fact, it is surprising in light of the teaching of the prior art that an additional carbon atom off the nitrogen would lead to the antibodies of the present invention.

Specifically with regard to Gross, the structures taught by Gross are phenethylamine derivatives. See column 3, structures (1)-(4), and column 6, structure (5). These structures all lack the N-ethyl substitution of the haptens, tracers, and immunogens of present invention, and Gross contains no teaching that would lead the skilled artisan to the N-ethyl-substituted derivatives of the present invention, nor does Gross teach the benefit of using N-ethyl

amphetamine derivatives to obtain antibodies specific for MDEA as taught by the present invention. It follows, therefore, that the antibodies, kits, and methods of the present invention are likewise neither anticipated nor made obvious by the disclosure of Gross.

Specifically with regard to Soares, the structures taught by Soares are phenethylamine derivatives. See column 3, structures (1)-(4), and column 6, structure (5). These structures all lack the N-ethyl substitution of the haptens, tracers, and immunogens of present invention, and Soares contains no teaching that would lead to the N-ethyl-substituted derivatives of the present invention, nor does Soares teach the benefit of using N-ethyl amphetamine derivatives to obtain antibodies specific for MDEA as taught by the present invention. It follows, therefore, that the antibodies, kits, and methods of the present invention are likewise neither anticipated nor made obvious by the disclosure of Soares.

Specifically with regard to Buechler, the structures taught by Buechler are amphetamine derivatives. See Figure 1, Example 15. These structures all lack the N-ethyl substitution of the haptens, tracers, and immunogens of present invention, and Buechler contains no teaching that would lead to the N-ethyl-substituted derivatives of the present invention, nor does Buechler teach the benefit of using N-ethyl amphetamine derivatives to obtain antibodies specific for MDEA as taught by the present invention. It follows, therefore, that the antibodies, kits, and methods of the present invention are likewise neither anticipated nor made obvious by the disclosure of Buechler.

Specifically with regard to Huber, the structures taught by Huber are amphetamine derivatives. See the structure at column 2, line 40, and Figure 2, structures 15-17. These structures are all maleimide derivatives, however, and further, Huber contains no teaching that would lead to the derivatives of the present invention, nor does Huber teach the benefit of using N-ethyl amphetamine derivatives to obtain antibodies specific for MDEA as taught by the present invention. It follows, therefore, that the antibodies, kits, and methods of the present invention are likewise neither anticipated nor made obvious by the disclosure of Huber.

Specifically with regard to Heiman, the structures taught by Heiman are amphetamine derivatives. See structures 7, 8, 12, and 13. These structures all lack the N-ethyl substitution of

the haptens, tracers, and immunogens of present invention, and Heiman contains no teaching that would lead to the N-ethyl-substituted derivatives of the present invention, nor does Heiman teach the benefit of using N-ethyl amphetamine derivatives to obtain antibodies specific for MDEA as taught by the present invention. It follows, therefore, that the antibodies, kits, and methods of the present invention are likewise neither anticipated nor made obvious by the disclosure of Heiman.

Specifically with regard to Hu, the structures taught by Hu are amphetamine derivatives. See the structure at column 4, line 25, and in claim 1. These structures lack the N-ethyl substitution of the haptens, tracers, and immunogens of present invention, and Hu contains no teaching that would lead to the N-ethyl-substituted derivatives of the present invention, nor does Hu teach the benefit of using N-ethyl amphetamine derivatives to obtain antibodies specific for MDEA as taught by the present invention. It follows, therefore, that the antibodies, kits, and methods of the present invention are likewise neither anticipated nor made obvious by the disclosure of Hu.

Specifically with regard to Byrnes, the structures taught by Byrnes are amphetamine derivatives. See the structures in Figs. 2B, 7, 9A, and 9D. These structures all lack the N-ethyl substitution of the haptens, tracers, and immunogens of present invention, and Byrnes contains no teaching that would lead to the N-ethyl-substituted derivatives of the present invention, nor does Byrnes teach the benefit of using N-ethyl amphetamine derivatives to obtain antibodies specific for MDEA as taught by the present invention. It follows, therefore, that the antibodies, kits, and methods of the present invention are likewise neither anticipated nor made obvious by the disclosure of Byrnes.

Specifically with regard to Schneider, the structures taught by Schneider are amphetamine derivatives. See column 2, line 50. These structures all lack the N-ethyl substitution of the haptens, tracers, and immunogens of present invention, and Schneider contains no teaching that would lead to the N-ethyl-substituted derivatives of the present invention, nor does Schneider teach the benefit of using N-ethyl amphetamine derivatives to obtain antibodies specific for MDEA as taught by the present invention. It follows, therefore, that the antibodies, kits, and methods of the present invention are likewise neither anticipated nor made obvious by the disclosure of Schneider.

Applicants argue that the examiners case for *prima facie* obviousness has not been made, and they respectfully request reconsideration of the rejection under 35 USC §103 (a).

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Applicants submit that their application is now in condition for allowance, and favorable reconsideration of their application in light of the above amendments and remarks is respectfully requested. Allowance of claims 1-3, 5-7, 10, 11, 13, 14, 16-33, and 36 at an early date is earnestly solicited.

The Examiner is hereby authorized to charge any fees associated with this Amendment to Deposit Account No. 02-2958. A duplicate copy of this sheet is enclosed.

Respectfully submitted,

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